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TREATMENT OF PRIMARY PNEUMONIC PLAGUE
BY THE COMBINED "COMPLEX" METHOD

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The first instances of curing cases of primary pneumonic plague by N. N. Zhukov-Verezhnikov's method took place in 1945. Pneumonic plague, particularly in its primary form, was considered incurable until recently. Every patient who had this disease was condemned to death; his remaining life span was measured in hours.

At present, the method of treating primary pneumonic plague, developed in detail by N. N. Zhukov-Verezhnikov, N. N. Ivanovskiy, T. D. Fadeyeva, and L. A. Uroda, gives the physician a powerful weapon for fighting this terrible disease. In 1945, the author witnessed the first cures of primary pneumonic plague by this method. He also observed the extensive experimental work on animals which was conducted before applying the method to humans.

Initially, Zhukov-Verezhnikov applied his method in the cases of three patients who had the disease and in a very severe form. After application of the first course of treatment, there was considerable improvement. Convalescence set in gradually and rather slowly. The dosage and intervals between administrations had not yet been determined with sufficient precision. However, the patients recovered, which showed that the principle of the treatment was right. Subsequently, the method of treatment was perfected on the basis of numerous laboratory analyses and clinical and X-ray investigations.

Extensive experience in the application of this method showed that interruption of the treatment or administration of drugs at the wrong time immediately brings about worsening of the patient's condition, so that there is danger of death. With correct prescription of remedies, the septic process, as a rule, is stopped within one month, and normal temperatures are then restored. The cardiovascular system remains in a labile state, however, which necessitates continued keeping of patients under observation.

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Let us describe the case of patient A. N., aged 65, who was treated by Dr Burdo. The author observed this case.

The patient had not been vaccinated and did not receive any remedies prior to the start of the disease. The disease took a very severe course, and the presence of large affected areas was detected in the lungs. A pure culture of *B. pestis* was isolated from the sputum.

Treatment of the patient was begun on the 2d day of the disease. A particularly severe condition was noted during the first 3 days. The temperature reached 39.5-40° C, and the patient complained about severe headaches, as well as pain in the chest and in the regions of the heart. There were occasional blackouts. After the remedies had been administered for the 4th day, the temperature of the patient dropped to 38°, and her general condition improved. However, on the 5th day the patient's temperature again went up to 38.5°, and her general condition became worse.

As a result of the treatment during the next 3 days (the 6th, 7th, and 8th days of the disease), the temperature began to drop gradually until it reached 36.5°, although the patient's condition was still very poor. On the 9th day the temperature again went up to 38.8°. The condition of the patient got worse, but during the next 6 days, i.e., the 10th-16th day of the disease, the temperature dropped again under the effect of the remedies and remained at the level of 36.8-37°. After the 16th day, the treatment was interrupted; the patient received serum only. As a result of the interruption in the administration (literally, introduction) of remedies, the patient's condition got worse rapidly. The temperature went up to 39.3°. The patient remained in this condition for 3 days. When the patient's condition became worse, treatment according to the standard procedure was resumed immediately. As a result, the patient's condition began to improve. However, the patient still felt ill for 15-20 days, constantly complaining about heart pains and general weakness.

I will not mention all cases of recovery of patients treated by this method, but will limit myself to describing only one further case in which a cure from primary pneumonic plague was brought about, namely that of the Chinese student F. He was a final-course student at the Mukden Medical Institute and was active in Manchuria as chief of a students' antiplague team. In the course of his work at a focus of plague infection, F. visited a patient without wearing complete protective clothing. In particular, he failed to put on protective goggles. The patient whom F. examined on this occasion had pneumonic plague in a severe form; he had a strong cough, and his sputum contained blood.

Two days after visiting this patient, F. became sick. His temperature rose rapidly and his breathing became rapid and difficult. He complained about pains in the region of the heart. In the chest there were dulling of sound on both sides and wet wheezes. Within 16-20 hr after the beginning of the disease, coughing, accompanied by discharge of sputum, set in. A large quantity of blood was contained in the sputum which was examined; a culture of plague bacilli could be isolated from it.

The students who worked with F. began to apply Zhukov-Verezhnikov's treatment. Although many of them were familiar with the principle of the method, they did not know all details. For that reason, they engaged the aid of USSR physician-specialists. The patient was treated by Dr Stepanova and a Chinese physician. Stepanova used the complete method as devised by Zhukov-Verezhnikov. Beginning with the first days of treatment, the patient felt considerable relief; the temperature dropped, his breathing became slower, and the wheezing in the chest diminished. However, the disease had been neglected, so that the patient began to feel worse after some improvement. Nevertheless,

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Dr Stepanova, being an able clinician, skillfully applied Zhukov-Verezhnikov's method and brought the patient out of his severe condition. The struggle for the life of the patient was hard, but Dr Stepanova succeeded in curing him after a fight which continued for 1.5 months.

At the expiration of 1.5 months, F.'s temperature dropped to a normal level and stayed there. No abnormal changes were noticeable any longer in the lungs and the patient began to feel well. A culture of plague bacilli could no longer be isolated from his sputum. In the next 3 months, during which F. was kept under our observation, his strength was restored gradually.

Let us dwell a little longer on the principles underlying the new method of treatment. A long study of the immunology of plague and of the pathogenesis of this disease preceded the development of the new method of treatment. In the course of extensive work by Zhukov-Verezhnikov and his collaborators, all basic immunological mechanisms and pathogenetic peculiarities of the plague infection were investigated. As a result, it was demonstrated that the organism of humans and animals is capable of developing an entirely effective immunity during the process of infection. However, the multiplication of plague bacilli is so rapid that immunological factors do not have time to assert themselves fully.

In 1940, N. N. Zhukov-Verezhnikov wrote. "In cases of plague, the condition which is unfavorable to the organism is brought about by the combined effect of the following circumstances.

- "1. Inadequate initial potential of normal factors of immunity and slow development of active immunity, which is explained by weak antigen activity.
- "2. High virulence and aggressiveness of *B. pestis*, the rates of multiplication and spreading of which greatly exceed the rate of development of active immunity.
- "3. Presence in *B. pestis* of toxic products and of Sanarelli-Schwartzmann factors, the action of which is unimpeded and leads to the organism's death before neutralizing antibodies had time to develop.

"The above demonstrates clearly why we attach so much importance to prolonging life in the treatment of plague. According to pessimistic views, which, by the way, are quite widespread, prolonging the life span of patients who have an acute form of plague does not testify to any success in serum therapy, because such patients die anyway. On comparing numerous published data with the results of our own observations and experiments, we arrived at the opposite conclusion. Thanks to serum therapy, the life of patients having primary pneumonic plague or acute forms of bubonic plague is prolonged to an increasing extent with every passing year. In the light of the hypothesis formulated above, which explains the fundamental reasons for the severe course of plague, one must reach the conclusion that the task to be solved in the course of further development of serum therapy consists precisely in prolonging the life span beyond the point past which active immunity of the organism begins to be exhibited."

Thus, all further work of the group was concentrated on finding and developing agents which would prevent multiplication and spreading of *B. pestis* in the organism. The task was to prolong life of patients having primary pneumonic plague beyond the limit after which active immunity of the organism begins to assert itself. Further investigations showed that none of the bacteriostatic agents known at the time, when taken alone would have impeded multiplication of the bacilli to the necessary extent. On the other hand, it was already

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established in 1944 that some chemotherapeutic agents which exhibit bacteriostatic action, also acquire bacteriocidal properties when used in complex combination. On this basis, use of the chemotherapeutic agents mentioned above was combined in the "complex" method of treatment.(2)

At the same time, antiplague serum was used to detoxify the organism. Beginning in 1947, streptomycin was included in the therapeutic procedure. This drug, as shown by the work of Korobkova, has a considerable bacteriostatic and anti-infectious action with reference to the plague bacterium. However, one must emphasize that even without the use of this drug complex treatment insures recovery from primary pulmonary plague. As a result of application of the complex method of treatment during 5 years, ideas held by physicians on the clinical aspects of primary pulmonary plague have been revised considerably.

By means of X-ray examinations, it was established that the glands at the roots of the lungs become involved during the second half of the period of disease, so that the threat of development of a new infection focus arises at that time. For this reason, it is necessary to continue the treatment during the second phase of the disease although the general conditions of patients shows considerable improvement. Clinical investigation also disclosed that the lungs show a tendency to develop abscesses. To eliminate this complication, a method of treatment with penicillin was devised.

Unity of theory and practice are typical of Zhukov-Verezhnikov's method and the line of investigation pursued by his group. In connection with the introduction of this method, the organizational aspects of work at plague foci were changed to take account of the necessity of beginning treatment as soon as possible and of administering remedies to infected persons who are still in the incubation period.

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